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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/846,033	04/30/2001	Edward Rebar	019496-005820US	4301

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EXAMINER
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SEHARASEYON, JEGATHEESAN

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 09/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/846,033	<b>Applicant(s)</b> REBAR ET AL.	
	<b>Examiner</b> Jegatheesan Seharaseyon	<b>Art Unit</b> 1647	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 01 July 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 67-71, 75, 77 and 95-103 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 67, 71, 75, 77, 95, 99 and 103 is/are rejected.
- 7) ☐ Claim(s) 68-70, 96-98 and 100-102 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. This Office Action is in response to Applicant's remarks and arguments filed on 7/1/2004. Claims 67-71, 75, 77 and 95-103 are pending. The finality of the rejection of the last Office Action mailed 18<sup>th</sup> 2004 is withdrawn.
2. The Office acknowledges the receipt of specification including SEQ ID Nos filed April 18<sup>th</sup> 2002.
3. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

#### ***Claim Rejections - 35 USC § 103, withdrawn***

4. The rejection of claims 67-71, 75 and 77 under 35 USC 103 (a) as being unpatentable over Ferrara et al. (1997) in view of Cox, III et al. (6, 534, 261) is withdrawn in light of Applicant's arguments with respect to Cox, III et al. reference <sup>not</sup> being available as prior art due to being commonly assigned to Sangamo Biosciences, Inc.

Applicant's arguments with respect to Ferrara's reference has been fully considered but are not found to be persuasive with respect to the administration of VEGF compared to zinc finger proteins as described in the instant invention for therapeutic purposes. As indicated previously in Office Actions mailed 5/18/2004 and 11/12/2003, the Office introduced Ferrara's teachings to indicate the modulation of VEGF gene in pathological conditions including angiogenesis. Specifically, Ferrara teaches the modulation of VEGF gene by transcriptional regulatory factor HIF-1 (see page: 7). Contrary to Applicants assertion that Ferrara reference is discussing the role of a naturally occurring transcription

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factor in a natural process, it should be noted that the reference also teaches the use of purified HIF-1 protein in the regulation (see page: 7, 2<sup>nd</sup> paragraph). Thus, providing the motivation to modulate VEGF gene by transcriptional factors.

Finally, Cox III reference was used to teach the use of zinc finger proteins. It should be noted that, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). However, since Cox III reference is no longer available as prior art the rejections of record are withdrawn.

Therefore, the rejections of record of claims 67-71, 75 and 77 under 35 USC 103 (a) as being unpatentable over Ferrara et al. (1997) in view of Cox, III et al. (6, 534, 261) is withdrawn.

5. The rejection of claims 95 and 96-103 under 35 USC 103 (a) as being unpatentable over Ferrara et al. (1997) and Baird et al. (6, 479, 654) in view of Cox, III et al. (6, 534, 261) is withdrawn in light of Applicant's arguments with respect to Cox, III et al. reference being available as prior art due to being commonly assigned to Sangamo Biosciences, Inc. Applicant's arguments with respect to Baird's reference has been fully considered but are not found to be persuasive with respect to wound healing. As indicated previously in Office Actions mailed 5/18/2004 and 11/12/2003 the Baird reference teaches role of VEGF modulation in tissue repair (wound healing). The Office has previously addressed the motivation and expectation of success presented in the

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combination of references (see page 4 and 5 of Office Action dated 5/18/2004). It should be noted that, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). However, since Cox III reference is no longer available as prior art the rejections of record are withdrawn. Therefore, the rejections of record of claims 95 and 96-103 under 35 USC 103 (a) as being unpatentable over Ferrara et al. (1997) and Baird et al. (6, 479, 654) in view of Cox, III et al. (6, 534, 261) is withdrawn.

***New Claim Rejections - 35 USC § 103***

6a. Claims 67, 71 and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pal et al. (1998) in view of Barbas, III et al. (U.S. Patent No: 6,140,466).

Pal et al. describe the transcriptional regulation of VEGF gene by transcription factor protein Sp1 (see abstract). The modulation of Sp1-dependent transcriptional regulation of VEGF thereby, modulates angiogenesis. However, Pal et al. does not teach the administration of zinc finger proteins to animals having a genome comprising a target site within a genome to modulate transcription.

Barbas, III et al. describe zinc finger proteins of the Cys<sub>2</sub>His<sub>2</sub> type that include Sp1 and containing at least three fingers of the C<sub>2</sub>H<sub>2</sub> class of zinc fingers (abstract). Barbas, III et al teaches that zinc finger proteins are broadly applicable as genome-specific transcriptional switches in therapeutics (abstract). This

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reference also provides a method of treating a subject with a cell proliferative disorder, wherein the disorder is associated with the modulation of gene expression associated with a zinc finger-nucleotide binding motif, comprising contacting the zinc finger-nucleotide binding motif with an effective amount of a zinc finger-nucleotide binding polypeptide derivative that binds to the zinc finger-nucleotide binding motif to modulate activity of the gene (column 3, lines 35-44). Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made to regulate VEGF gene in order to regulate angiogenesis as described by Pal et al. by introducing a zinc finger protein (like Sp1) into an animal to target a site within VEGF gene as taught by Barbas III et al., with the expectation of modulating the expression of VEGF gene. One of ordinary skill in the art would have been motivated to modulate angiogenesis by regulating the expression of VEGF gene by introducing zinc finger protein to target a site on VEGF gene to regulate the VEGF gene expression as taught by Pal et al. Therefore, the instant claims are *prima facie* obvious over Pal et al. (1998) in view of Barbas, III et al. (U.S. Patent No: 6,140,466).

6b. Claim 75, 95, 99 and 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pal et al. (1998) in view of Barbas, III et al. (U.S. Patent No: 6,140,466) and Baird et al. (U.S. Patent No: 6,479, 654).

The instant invention is directed to modulating angiogenesis by introducing zinc finger protein into an animal to a target site on VEGF gene. It is also directed to treating wound healing.

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The teachings of Pal et al. and Barbas III et al. have been described above in paragraph 6a. However, the references do not recite the role of VEGF in wound healing. Baird et al. teach that the up regulation of VEGF after hypoxia is essential for wound healing (column 3, lines 1-5) and ischemia (column 3, lines 10-30 and column 9, lines 5-20). It also teaches topical administration of composition (column 21, lines 30-33). It also contemplates a method of achieving tissue specific expression (column 24, lines 37-44). Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made to modulate the VEGF gene as described by Pal et al. by introducing a zinc finger protein into an animal to target a site within VEGF gene as taught by Barbas, III et al. with the expectation of up regulating the VEGF gene expression to treat tissue repair (wound healing) and ischemia as described by Baird et al. One of ordinary skill in the art would have been motivated to modulate angiogenesis by regulating the expression of VEGF gene by introducing zinc finger protein to target a site on VEGF gene to modulate the VEGF gene expression as taught by Pal et al. In addition, regulating VEGF expression will enable one to treat conditions such as wound healing and ischemia as described in Baird et al. Therefore, the instant claims are *prima facie* obvious over Pal et al. (1998) in view of Barbas, III et al. (U.S. Patent No: 6,140,466) and Baird et al. (U.S. Patent No: 6,479, 654).

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7. Claims 68, 69, 70, 96, 97, 98, 100, 101 and 102 are objected to as dependent on rejected claims. However, these claims if rewritten as independent claims with the present limitations will be allowable over prior art.

**Contact Information**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS 09/04

  
**JANET ANDRES**  
**PRIMARY EXAMINER**